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1: Pharm Res 1994 Jul;11(7):1016-22 Related Articles, Books

Polystyrene-poly (ethylene glycol) (PS-PEG2000) particles as model systems for site specific drug delivery. 2. The effect of PEG surface density on the in vitro cell interaction and in vivo biodistribution.

Dunn SE, Brindley A, Davis SS, Davies MC, Illum L.

Department of Pharmaceutical Sciences, University of Nottingham, University Park, U.K.

The effect of differing densities of poly (ethylene glycol-2000) (PEG2000) at the particle surface of polystyrene-poly (ethylene glycol-2000) (PS-PEG2000) particles was assessed in terms of hydrophobic interaction chromatography (HIC) and the in vitro and in vivo behaviour of the particles. The particles, with different surface densities of PEG, were prepared by varying the copolymerizing reaction of styrene with a PEG macromonomer. There is a clear relationship between the surface density of PEG as determined by X-ray photoelectron spectroscopy and surface hydrophobicity as assessed by hydrophobic interaction chromatography (HIC). Similarly, the interaction of the particles with non-parenchymal liver cells in in vitro studies was shown to decrease as the surface density of PEG increases. The in vivo study investigating the biodistribution of the PS-PEG particles after intravenous injection into rats reveals that a relationship exists between the surface density of PEG and the extent to which the particles remain in the circulation, avoiding recognition by the reticuloendothelial system. Particles with the higher surface densities show increased circulatory times which compared well with data for particles prepared with the surface adsorbed PEO-PPO block copolymer, Poloxamine 908.

PMID: 7937542 [PubMed - indexed for MEDLINE]

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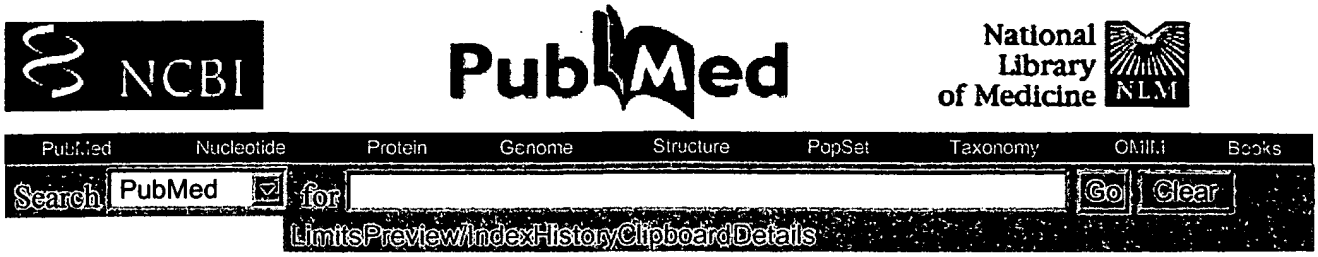
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1: Pharm Res 1993 Jul;10(7):970-4 Related Articles, Books

Biodistribution of micelle-forming polymer-drug conjugates.

Kwon GS, Yokoyama M, Okano T, Sakurai Y, Kataoka K.

International Center for Biomaterials Science, Science University of Tokyo, Chiba, Japan.

Polymeric micelles have potential utility as drug carriers. To this end, polymeric micelles based on AB block copolymers of polyethylene oxide (PEO) and poly(aspartic acid) [p(Asp)] with covalently bound Adriamycin (ADR) were prepared. The micelle forming polymer-drug conjugates [PEO-p(Asp(ADR)] were radiolabeled and their biodistribution was investigated after intravenous injection in mice. Long circulation times in blood for some compositions of PEO-p[Asp(ADR)] conjugates were evident, which are usually atypical of colloidal drug carriers. This was attributed to the low interaction of the PEO corona region of the micelles with biocomponents (e.g., proteins, cells). Low uptake of the PEO-p(Asp(ADR)] conjugates in the liver and spleen was determined. The biodistribution of the PEO-p[Asp(ADR)] conjugates was apparently dependent on micelle stability; stable micelles could maintain circulation in blood, while unstable micelles readily formed free polymer chains which rapidly underwent renal excretion. Long circulation times in blood of PEO-p(Asp(ADR)] conjugates are thought to be prerequisite for enhanced uptake at target sites (e.g., tumors).

PMID: 8378259 [PubMed - indexed for MEDLINE]

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1: Cancer Res 1990 Mar 15;50(6):1693-700 Related Articles, Books

Characterization and anticancer activity of the micelle-forming polymeric anticancer drug adriamycin-conjugated poly(ethylene glycol)-poly(aspartic acid) block copolymer.

Yokoyama M, Miyauchi M, Yamada N, Okano T, Sakurai Y, Kataoka K, Inoue S.

Institute of Biomedical Engineering, Tokyo Women's Medical College, Japan.

Adriamycin (ADR), an anthracycline anticancer drug, was bound to the poly(aspartic acid) chain of poly(ethylene glycol)-poly(aspartic acid) block copolymer by amide bond formation between an amino group of Adriamycin and the carboxyl groups of the poly(aspartic acid) chain. The polymeric drug thus obtained was observed to form a micelle structure possessing diameter of approximately 50 nm, with a narrow distribution, in phosphate-buffered saline and to show excellent water solubility despite a large amount of ADR introduction. Further, it was able to be stored in lyophilized form without losing its water solubility in the redissolving procedure. Increased stability of the bound Adriamycin molecules in phosphate-buffered saline and elimination of binding affinity for bovine serum albumin due to the micelle formation were further advantages of this polymeric drug. In vivo high anticancer activity of this micelle-forming polymeric drug against P 388 mouse leukemia was obtained with less body weight loss than that seen with free ADR, due to low toxicity as compared with free ADR.

PMID: 2306723 [PubMed - indexed for MEDLINE]

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1: J Pharm Sci 1996 Jan;85(1):85-90

Preparation and characterization of the micelle-forming polymeric drug indomethacin-incorporated poly(ethylene oxide)-poly(beta-benzyl L-aspartate) block copolymer micelles.

La SB, Okano T, Kataoka K.

International Center for Biomaterials Science, Science University of Tokyo, Chiba, Japan.

To estimate the feasibility of novel containers for drugs, poly(ethylene oxide)-poly(beta-benzyl L-aspartate) (PEO-PBLA) micelles were prepared by dialysis against water using different solvents. The solvent selected is very important because it drastically affects the stability of polymeric micelles. The critical micelle concentration (cmc) of the prepared micelles in distilled water was determined by a fluorescence probe technique using pyrene. Indomethacin (IMC) as a model drug was incorporated into the micelles by dialysis and an oil/water emulsion method. Characteristics of PEO-PBLA micelles without and with the physically trapped IMC in the inner core of the micelles (IMC/PEO-PBLA) were studied by dynamic light scattering and gel permeation chromatography/HPLC as well as an in vitro release test of IMC from the micelles. For the PEO-PBLA block copolymers, N,N-dimethylacetamide (DMAc) was found to be the best of the solvents tested to form stable polymeric micelles with a narrow size distribution and avoid its aggregation, and the cmc of PEO-PBLA micelles thus prepared was determined to be ca. 18 mg/L in water. The diameters of PEO-PBLA micelles and IMC/PEO-PBLA micelles in number averaged scale were observed to be ca. 19 and 25-29 nm, respectively. The release study of IMC from IMC/PEO-PBLA micelles in various buffer solutions at the pH range from 1.2 to 7.4 at 37 degrees C revealed that the release rate of IMC from the micelles was increased by increasing the pH of the medium and indicated that the release rate of IMC from the micelles are controlled by the partition coefficient of IMC based on the pH of the medium and interaction between IMC and the hydrophobic portion of the

micelles.

PMID: 8926590 [PubMed - indexed for MEDLINE]